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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/465,133	12/15/1999	ELISABETTA VEGETO	246/180	8491
25746	7590	03/16/2005	EXAMINER	
WONG CABELLO LUTSCH RUTHERFORD & BRUCCULERI, LLP 20333 SH 249, SUITE 600 HOUSTON, TX 77070			QIAN, CELINE X	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 03/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/465,133	Applicant(s) VEGETO ET AL	
	Examiner Celine X. Qian Ph.D.	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 April 1213.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 144,147,148,150-161,163-168 and 170-192 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 144,147,148,150-161,163-168 and 170-192 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 January 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>12/13/04</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Claims 144, 147, 148, 150-161, 163-168, 170-192 are pending in the application.

This Office Action is in response to the Amendment filed on 12/13/04.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/13/04 has been entered.

Response to Amendment

The rejection of claims 144, 147, 148, 150-161, 163-168, 170-192 under 35 U.S.C. 112 1st paragraph (written description and scope of enablement) is maintained for reasons set forth of the record mailed on 7/13/04 and further discussed below.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 144, 147, 148, 150-161, 163-168, and 170-192 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to

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reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants did not respond to this rejection. As such, this rejection is maintained for same reason as set forth in the office action mailed on 7/13/04. Briefly, the claims encompass a genus of molecular switches that comprises a non-steroid hormone receptor DNA binding domain which binds a promoter that is transcriptionally linked to a target gene; a mutated progesterone receptor ligand binding domain which is distinct from a naturally occurring ligand binding domain by one or more alterations in from about 1 to about 54 naturally occurring carboxyl terminal amino acids. The claimed genus potentially encompasses a large number of mutated progesterone receptor from various species having one or more alteration in the 1-54 C' terminal amino acid region. However, the specification only discloses two deletion mutations of the human progesterone receptor that has the molecular switch function as claimed. The specification fails to teach other types of mutation such as substitution or insertion within this region that would also create the molecular switch as claimed. Moreover, the specification fails to describe progesterone receptors from other species having mutations within this region that have the same "molecular switch" function. As such, the specification fails to describe a representative number of species by their complete structure or other identifying characteristics. Therefore, the written description requirement for the claimed genus of "molecular switch" is not satisfied.

Claims 144, 147, 148, 150-161, 163-168, 170-192 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of regulating gene

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expression transiently *in vivo* by either a) introducing into a wild type animal a construct encoding the human progesterone receptor with at least 42 amino acid deletion from C-terminal, and another construct comprising a progesterone receptor responsive element linked to a report gene; b) administering a ligand that binds to said mutated receptor to said animal, or administering a ligand that binds to said mutated human progesterone receptor to a transgenic non-human animal, wherein said transgenic non-human animal expresses a heterologous reporter gene and said mutated human progesterone receptor, wherein expression of said receptor regulates the expression of the reporter gene by binding to the promoter of said reporter gene, does not reasonably provide enablement for said method utilizing any transgenic animal or long term expression in any animal, and/or any mutated steroid hormone receptor that is capable of binding ligand that is an antagonist of the natural occurring receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In response to this rejection, Applicants argue that undue experimentation would not be required to identify further deletions or substitutions in this region that would provide the same result as the surprising discovery of modification of the amino acid sequence in the final 54 C' region would convert an antagonist of the naturally occurring receptor into an antagonist.

Applicants argue that the finding of deletion of the 54 C' terminal amino acid abolishes progesterone binding and allowing antiprogestins to have agonist effect is sufficient for one with high skill in the art to generate other mutations in the C' terminal region that destroyed progesterone binding while retaining the antiprogestin effect. Applicants thus conclude that the claimed invention is enabled to its full scope.

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The above arguments have been fully considered but deemed unpersuasive. The reasons of non-enablement for the claimed invention is set forth in the office action mailed on 7/13/04. As discussed in the previous office action, the examiner acknowledges that 54 and 42 amino acid deletions from the C-terminal of progesterone receptor are taught in the specification, however, whether mutation of any kind (including single substitution, deletion of 1 or 2 amino acid from this region) of 1-54 amino acid in this region would result in the molecular switch as claimed is unpredictable. Furthermore, the specification fails to teach whether deletion of 1-54 amino acid from progesterone receptor of other species would also result in the molecular switch as claimed. The specification does not teach whether other mutation within this region of the human progesterone receptor can result in the claimed molecular switch. The specification also fails to teach whether mutations within 1-54 C' amino acid of progesterone receptor from other species would result in the claimed molecular switch. The art does not teach such information either. As such, without teaching from the specification and the prior art, one of skilled in the art would have to engage in undue experimentation to make and use the claimed invention to its full scope.

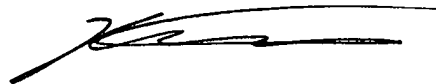
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.
Examiner
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A handwritten signature in black ink, appearing to read 'Celine X Qian', with a long horizontal flourish extending to the right.

**CELIAN QIAN
PATENT EXAMINER**